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APPENDIX A

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APPENDIX B

Bibliographic Information

Animal models in the preclinical assessment of therapy for viral hepatitis. Tennant, Bud C.; Baldwin, Betty H.; Hornbuckle, William E.; Korba, Brent E.; Cote, Paul J.; Gerin, John L. College of Veterinary Medicine, Cornell University, Ithaca, NY, USA. *Antiviral Therapy* (1996), 1(Suppl. 4, Therapies for Viral Hepatitis), 47-52. CODEN: ANTHFA ISSN: 1359-6535. Journal; General Review written in English. CAN 126:271668 AN 1997:228418 CAPLUS (Copyright 2002 ACS)

Abstract

A review with 18 refs. Chronic infection with hepatitis B virus (HBV) represents a major cause of chronic hepatitis, cirrhosis of the liver and hepatocellular carcinoma in humans. Naturally acquired infections with other members of the hepadnavirus family have been observed in the Eastern woodchuck, California ground squirrel and Pekin duck, and all three species have been used for antiviral drug development. Woodchucks with chronic woodchuck hepatitis virus (WHV) infection develop progressively severe chronic hepatitis and hepatocellular carcinoma, diseases that are similar to those associated with persistent HBV infection. The availability of lab.-reared woodchucks free of several diseases that are endemic in wild woodchucks, combined with specific, sensitive serological markers of WHV infection and standardized inocula, have allowed this species to become a useful animal model of HBV infection and disease. Studies of a series of nucleoside analogs have shown a good correlation between in vitro activity against HBV using the 2.2.15 cell line and in vivo activity against WHV in the woodchuck model. Correlation has also been shown between humans and woodchucks in both antiviral activity and toxic effects of nucleoside analogs and immune response modifiers in chronic hepadnavirus infection. These observations demonstrate the value of the woodchuck for preclinical antiviral drug development and suggest that chronic WHV-carrier woodchucks should be useful in predicting the influence of long-term antiviral therapy on the outcome of chronic HBV infection in humans.